**I. Remarks**

Claims herein under examination are claims 7-11 and claim 25.

Claims 7 and 11 have been amended; no new matter has been added by this amendment. Support for the amendment to claims 7 and 11 is found throughout the application and particularly at page 36, lines 8-13. Claim 22 has been canceled without prejudice.

**II. Claim rejections under 35 U.S.C. § 112, First Paragraph**

A. Claims 7-10, 22, and 25 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. It is alleged that the claim(s) contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Specifically, the Office has alleged that the limitation in claim 7, which recites "a self-assembling fusion polypeptide wherein said fusion polypeptide (i) is capable of forming a stable homomultimer", is not supported by the specification or claims as originally filed. The Office concludes that this feature constitutes new matter. This conclusion rests on the assertion that the fusion polypeptide is not a homomultimer because the chains are not identical to one another. Applicants respectfully traverse because the homomultimers of the instant invention are made up of two identical polypeptide chains that self-assemble to form the multimer.

The claimed polynucleotide encodes for a fusion polypeptide that is a single polypeptide chain comprising two distinct domains- a T cell antigen presenting domain and an oligomerization domain. Upon expression of this polypeptide, the polypeptide chains will self-assemble with one another through the oligomerization domain to form homomultimers. These homomultimers are therefore comprised of two identical polypeptide chains; each chain has the same T cell antigen presenting domain and oligomerization domain.

Applicants point to the specification at page 36, lines 8-14:

> "The fusion polypeptides of the invention can form multimers spontaneously, without the need for chemical modifications, by self-assembly of the oligomerization domain or by binding of the an oligomerization domain to a second platform molecule. For example, if the oligomerization domain is a self-assembling molecule such as a leucine zipper, the fusion polypeptides will spontaneously form dimers in a solution with an appropriate salt concentration and pH. If the

oligomerization domain is a polypeptide factor that forms homotetramers, the fusion polypeptide will form tetramers."

To clarify this feature, Applicants have amended claim 7. Accordingly, Applicants assert that the rejected limitation in claims 7-10 and 26 does not represent new matter. The original specification and claims fully support the feature. Withdrawal of this rejection is therefore respectfully requested.

B. Claims 7-11 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. It is alleged that the claim(s) contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Specifically, the Office has alleged that the genus of self-assembling peptides is large and that Applicants have only disclosed leucine zippers as the "self-assembling" oligomerization domains As such, the Office alleges that Applicants were not in possession of the claimed invention as claimed. Applicants respectfully traverse.

Applicants have amended claims 7 and 11 to specify that the oligomerization domain comprises a leucine zipper. Therefore, this rejection is moot. Applicants respectfully request that the written description rejection be withdrawn and the claims be allowed to issue.

**III. Claim rejections under 35 U.S.C. § 102(b)**

Claims 7-10 and 22 stand rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Scott et al., *J. Exp. Medicine* 183:2087-2095 (1996) referred to hereafter as 'Scott". Applicants respectfully traverse. The instant claims are directed to a polynucleotide, which upon expression, produces fusion polypeptides that self-assemble to form a homomultimer made up of two identical polypeptide chains. In contrast, the Scott reference teaches a polynucleotide system encoding for polypeptides which are only capable of forming heterodimers, i.e. where two different polypeptide chains self-assemble.

As Applicants have set forth above, the claimed polynucleotide encodes for a fusion polypeptide that is a single polypeptide chain comprising two distinct domains- a T cell antigen presenting domain and a leucine zipper oligomerization domain. Upon expression of this fusion polypeptide, the expressed polypeptide chains will self-assemble through the leucine zipper domain to form homomultimers. These

homomultimers are therefore comprised of two identical polypeptide chains; each chain has the same T cell antigen presenting domain and leucine zipper domain.

In contrast, Scott discloses a fusion polypeptide incapable of forming a homomultimer. The reference examines the effect of enhanced murine MHC IA α and IA β chain pairing on the production of secreted MHC $IA^d$ molecules. To accomplish this, both MHC IA chains (α and β) were modified to include a complementary leucine zipper at their respective COOH terminus. These complementary leucine zippers force the association of the IA α and β chains. (See page 2087, 1st paragraph, last sentence; and 2nd paragraph, third sentence.) Figure 1A illustrates these polynucleotide constructs with the two different MHC IA chains and complementary leucine zippers (see page 2089, Figure 1A under "Modified cDNAs".) Expression of these polynucleotides produces polypeptides that associate to form only the paired, heterodimeric product (i.e. an IA α chain will not bind to another IA α chain.)

> "Since each chain is engineered to have a COOH-terminal peptide of opposite charge, the addition of the zipper produces only the correctly paired heterodimeric product." (Scott et al., page 2089, 1st full paragraph, third sentence.)

Therefore, the polynucleotides taught by the Scott reference does not and cannot produce a homomultimer as required in claim 7, step (ii).

As noted by the Office on page 5 of the Office Action mailed June 21, 2004, Applicants did set forth the position that Applicants' entire fusion polypeptide will form a homomultimer as a result of the oligomerization domain because it is a single polypeptide molecule. This is true for the instant invention. The fusion polypeptides that self-assemble are identical polypeptide chains and will thus form homomultimers comprised of two identical fusion polypeptides when they self-assemble. In contrast, the fusion polypeptides taught in Scott will also form multimers but they will only form heteromultimers, not homomultimers. This is because the Scott polypeptides that self-assemble are not identical to one another. They each have a different T cell antigen presenting domain, an MHC IA α chain or an MHC IA β chain, which is fused to a leucine zipper domain. The claimed invention requires a polynucleotide encoding for a fusion polypeptide capable of forming homomultimers by self-assembly via the oligomerization domain. Therefore, the Scott reference does not anticipate the instant invention. Withdrawal of this rejection is respectfully requested.

**IV. Claim Amendments under 37 C.F.R. § 1.121**

1. (Withdrawn) A method for inducing an immune response to an endogenous antigen in a subject comprising delivering a cytotoxic agent,

wherein said cytotoxic agent is an effective amount of one or more of herpes simplex virus thymidine kinase (HSV-tk), gancicolvir, or a rejection antigen, that stimulates *in vivo* loading of an endogenous antigen,

wherein said endogenous antigen is a tumor associated antigen or a viral antigen, into an antigenic binding protein (APBP) molecule, wherein said APBP molecule is selected the group consisting of a heat shock protein (HSP), a soluble major histocompatibility complex (MHC) class I molecule, an antigen presenting matrix, a multimer of soluble MHC class I molecules and an antibody engineered to bind antigen peptides, under conditions so that the endogenous antigen is presented to a T cell and the agent induces lysis of said target cell.

2. (Withdrawn) A method for inducing lysis of a target cell in a subject, comprising the steps of:

a. inducing an immune response to an exogenous rejection antigen in the subject, comprising (I)delivering to the subject an effective amount of a composition comprising the exogenous rejection antigen that presents the exogenous rejection antigen on the cell surface, or (ii)delivering to the subject an effective amount of an immune effector cell population educated with the exogenous rejection antigen; and

b. delivering to a target cell, wherein the target cell is a tumor cell or a virally infected cell, in the subject an effective amount of a polynucleotide encoding the exogenous antigen, thereby inducing lysis of the target cell in the subject.

3. (Withdrawn) The method of claim 2 further comprising delivering an effective amount of an antigen presenting cell recruitment factor.

4. (Withdrawn) A fusion polypeptide comprising a T cell antigen presenting domain fused to an oligomerization domain.

5. (Withdrawn) The fusion polypeptide of claim 4, wherein the T cell antigen presenting domain comprises a plurality of immunoglobulin fold domains of an MHC class I molecule.

6. (Withdrawn) The fusion polypeptide of claim 4 wherein the oligomerization domain is selected from the group consisting of a peptide mimetic of a ligand, and a self-assembling protein.

7. (Currently amended) An isolated polynucleotide comprising a nucleic acid sequence encoding a self-assembling fusion polypeptide wherein said fusion polypeptide

(i) is capable of forming a stable homomultimer by self-assembly of the leucine zipper domain and,

(ii) comprises a T cell antigen presenting domain of an MHC molecule fused to a [[n]] leucine zipper ~~oligomerization~~ domain.

8. (Original) A gene delivery vehicle comprising the polynucleotide of claim 7.

9. (Original) A host cell comprising the polynucleotide of claim 7.

10. (Previously presented) A host cell comprising the polypeptide expressed from the polynucleotide of claim 7.

11. (Currently amended) A recombinant system comprising:

(i) a first polynucleotide comprising a nucleic acid sequence encoding a fusion polypeptide, wherein said fusion polypeptide comprises a T cell antigen presenting domain of an MHC molecule fused to a[[n]] ~~oligomerization~~ leucine zipper domain, and

(ii) a second polynucleotide comprising a nucleic acid sequence encoding T cell epitope which binds specifically to the antigen presenting domain of the fusion polypeptide.

12. (Withdrawn) A method of producing an antigen presenting multimer comprising expressing a recombinant system comprising the isolated polynucleotide of claim 7 and a second polynucleotide that encodes a T cell epitope, said T cell epitope selected from the group consisting of a tumor cell antigen, a pathogenic antigen, and a self-antigen, which binds specifically to the antigen presenting domain of the fusion polypeptide, under conditions which allow the formation of antigen presenting multimers and isolating the multimer.

13. (Withdrawn) A method of detecting an antigen specific T cell comprising contacting peripheral blood lymphocytes with antigen presenting multimers of claim 12 under conditions which allow antigen specific binding to T cells, and detecting the multimer-T cell complex.

14. (Withdrawn) A method of isolating an antigen specific T cell comprising purifying the antigen specific T cells of claim 13.

15. (Withdrawn) The T cell isolated by the method of claim 14.

16. (Withdrawn) A method of expanding a population of antigen specific T cells comprising culturing the cell of claim 15.

17. (Withdrawn) The T cell population expanded by the method of claim 16.

18. (Withdrawn) A method of enhancing an immune response in a subject comprising administering to the subject an expanded population of antigen specific T cells of claim 17.

19. (Withdrawn) An isolated polynucleotide comprising a nucleic acid sequence encoding a fusion polypeptide, wherein said fusion polypeptide comprises:

a T cell antigen presenting domain fused to an oligomerization domain, wherein said oligomerization domain:

(a) will not bind to itself and,

(b) is capable of non-covalently binding to a multivalent platform molecule that has multiple binding sites, and

wherein the combination of said fusion polypeptide and the multivalent platform molecule form a stable multimer.

20. (Withdrawn) The isolated polynucleotide of claim 19, wherein the oligomerization domain is selected from the group consisting of a ligand which binds to a receptor molecule, a peptide mimetic of a ligand, and a substrate binding domain.

21. (Withdrawn) The isolated polynucleotide of claim 20, wherein the substrate binding domain is selected from the group consisting of a peptide mimetic of biotin and a heparin binding domain.

22. (Canceled)

23. (Withdrawn) A gene delivery vehicle comprising the polynucleotide of claim 19.

24. (Withdrawn) A host cell comprising the polynucleotide of claim 19.

25. (Previously presented) A recombinant system comprising:

(i) a first polynucleotide comprising a nucleic acid sequence encoding a fusion polypeptide, wherein said fusion polypeptide comprises a T cell antigen presenting domain of an MHC molecule fused to an oligomerization domain comprising a leucine zipper domain, and

(ii) a second polynucleotide comprising a nucleic acid sequence encoding T cell epitope which binds specifically to the antigen presenting domain of the fusion polypeptide.

**V. Conclusion**

No fee is deemed necessary in connection with the filing of this communication. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposi. Account No. 07-1074.

Respectfully submitted,

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